

OVERVIEW OF CHLORPYRIFOS REVISED RISK ASSESSMENT

Introduction

This document summarizes EPA's human health and ecological risk findings and conclusions for the organophosphate pesticide chlorpyrifos as presented fully in the document, "Revised Human Health Risk Assessment for Chlorpyrifos" dated June 8, 2000, and "Revised EFED Risk Assessment for the Reregistration Eligibility Decision on Chlorpyrifos," dated June 2000. The purpose of this overview is to assist the reader by identifying the key features and findings of these risk assessments, and to better understand the conclusions reached in the assessments. This overview was developed in response to comments and requests from the public which indicated that the risk assessments were difficult to understand, that they were too lengthy and that it was not easy to compare the assessments for different chemicals due to the use of different formats.

The revised human health and ecological risk assessments for chlorpyrifos along with the overview and summary of the assessments will be posted on the Internet (<http://www.epa.gov/pesticides/op/chlorpyrifos.htm>) and placed in the Pesticide Docket on June 8, 2000. A 60-day public participation period on risk management will begin with the publishing of a federal register notice announcement.

EPA has determined that it is appropriate to treat the organophosphates (OPs) as sharing a common mechanism of toxicity: the inhibition of cholinesterase activity. As required by the Food Quality Protection Act (FQPA), a cumulative assessment will need to be conducted to evaluate the risk from food, water and non-occupational exposure resulting from all uses of OPs. Currently, the Agency is developing the draft methodology needed to conduct such an assessment with guidance/advice provided by the Science Advisory Panel. This draft methodology will be available for public comment when it is completed. Consequently, the risks summarized in this document are only for chlorpyrifos.

Use Profile

Currently Registered Uses:

- **Insecticide:** Registered for use on the following crops/sites: cranberries, strawberries, citrus, apples, figs, pears, nectarines, cherries, peaches, plums, grapes, almonds, pecans, walnuts, onions, peppers, kale, broccoli, brussels sprouts, cabbage, cauliflower, collards,

cucurbits, asparagus, roots/tubers, corn, tomatoes, lentils, beans, peas, sorghum, tobacco, wheat, alfalfa, peanuts, soybeans, sunflower, cotton, sugar beets, mint, bananas, pasture, woodland, and lots/farmsteads. Chlorpyrifos is also used as a termiticide, mosquitocide, treatment for lawns, turf and ornamentals, indoor crack and crevice and spot treatment, in pet collars, in cattle eartags, and in several other miscellaneous uses such as in manholes.

Post-Mitigation Uses:

- As part of mitigation, the following use changes have been agreed upon:
 - Eliminating use on tomatoes and revoking the associated tolerance;
 - Restricting use on apples to pre-bloom (dormant) applications;
 - Eliminating all indoor residential uses (except fully contained ant baits in child resistance packaging).
 - Eliminating all outdoor residential uses (except limited public health uses).
 - Eliminating all indoor and outdoor non-residential uses except:
 - Use on golf courses
 - Limited public health uses (i.e. mosquito control and fire ant mounds)
 - Limited use in industrial settings (e.g. manufacturing plants, ship holds)
 - Eliminating whole house “post-construction” termiticide use.
 - Phasing out limited post-construction spot and local termiticide treatments by 2002.
 - Phasing out pre-construction termiticide treatments by 2005.
- In addition to these agreed upon actions the Agency will also propose to revoke the tolerance on tomatoes and reduce the tolerances on apples and grapes to 0.01 ppm which reflect the mitigated use patterns.
- **Formulations:** Formulated as a liquid emulsifiable concentrate, granular, wettable powder, dry flowable, pressurized liquid, dust, ready-to-use solution, microencapsulated material, pellets/tablets, soluble concentrate and as an impregnated material (eartag and pet collar).
- **Method of Application:** Applied by aerial, chemigation, groundboom, tractor-drawn granular spreader, airblast sprayer, low and high pressure hand wands, hydraulic hand-held sprayer, shaker can, bulbous duster, belly grinder, push-type spreader, large tank sprayer, compressed air sprayer, hose-end sprayer, aerosol sprayer, hand, and in pet collars and eartags.
- **Use Rates:** Maximum application rates range from 0.5 lb/ai/A to 8 lb/ai/A (sodfarm). The number of applications per year generally range from 1 to 8. Cherries, macadamia nuts, peppers and tomatoes can have up to 8 applications per year. Up to 10 applications are permissible in some citrus growing areas (grove floor treatment).

- **Annual Poundage:** Estimates for total usage in the U.S. range from approximately 20 million (average) to 24 million (maximum) lbs a.i./year. Approximately 48% of chlorpyrifos is used in agricultural settings and 52% is used in PCO/turf/residential markets. Crops with the highest % crop treated (CT) are cranberries (46%), apples (44%), broccoli (41%), brussels sprouts (33%) and cauliflower (31%). In terms of total pounds a.i., two crops corn (27%) and cotton (3%), account for the greatest agricultural use. Termite control (24%) and turf (12%) account for the largest non-agricultural markets (in terms of pounds a.i.) for chlorpyrifos. Further, 24% of food handling establishments are treated with chlorpyrifos.
- **Technical Registrants:** Dow AgroSciences, Cheminova, Mahkteshim-Agan, Gharda, Platte Chemical, and Luxembourg-Pamol .

Human Health Risk Assessment

FQPA Safety Factor Determination

In March 1999, the Agency concluded that a 3X FQPA safety factor should be retained for chlorpyrifos due to concern for increased sensitivity seen at high doses in a literature study and for the qualitative increased susceptibility occurring at the high dose in the developmental neurotoxicity (DNT) study.

In February 2000 this decision was revisited due to the availability of new data. In the new data:

- increased sensitivity following a single oral exposure to neonates was seen at substantially lower doses; and
- a clear qualitative difference in response (i.e., susceptibility) between adult rats and their offspring was demonstrated in new data related to the developmental neurotoxicity study.
- a suggestion that the inhibition of cholinesterase may not be essential for adverse effects on brain development was seen; and
- an offspring NOAEL in the DNT, based upon structural alterations in brain development as the toxicity endpoint of concern, was not demonstrated.

Therefore, the Agency concluded that the available hazard and exposure databases for chlorpyrifos, including the information received and reviewed in the past year, result in an overall *higher* degree of concern regarding the potential consequences of chlorpyrifos exposure to infants and children than was determined during the FQPA safety factor evaluation in March 1999. Consequently, the Agency has concluded that the FQPA safety factor should be retained at 10X.

The Agency determined that the FQPA safety factor would be applicable to females 13-50 and Infants and Children population subgroups for all exposure durations.

Acute Dietary (Food) Risk

Acute dietary risk is calculated considering what is eaten by individuals in one day and residue values for food. This assessment was refined using probabilistic methods (Monte Carlo) which take into account the full range of consumption and residue values. A risk estimate that is less than 100% of the acute Population Adjusted Dose (aPAD) (the dose at which an individual could be exposed on any given day and no adverse health effects would be expected) does exceed the Agency's risk concern. The aPAD is the acute reference dose (aRfD) adjusted for the FQPA safety factor.

- **Based on all currently registered uses (pre-mitigation):** At the 99.9th percentile, for the most highly exposed population sub-group, children 1-6, 355% of the aPAD is occupied. This exceeds the Agency's level of concern. See Table 1.
- The major contributors to exposure, or "risk drivers", based on currently registered uses are apples (residues resulting from post-bloom uses), grapes (residues primarily on imported crops) and fresh tomatoes.
- Acute dietary risk concerns are mitigated by:
 - Eliminating use on tomatoes and revoking the associated tolerance;
 - Restricting use on apples to pre-bloom (dormant) applications and reducing the tolerance to 0.01 ppm to reflect this new use pattern;
 - Reducing the tolerance on grapes to 0.01 ppm to reflect the domestic use pattern.
- **Post-mitigation:** At the 99.9th percentile, the dietary risk, food only, is below levels of concern for all population sub-groups, including the most sensitive population sub-group, children 1-6 years-old, which is at 82% of the aPAD. See Table 1.

TABLE 1: Chlorpyrifos: Risk Estimates as a Percentage of the Acute PAD (% aPAD)

Subpopulation	Pre-Risk Mitigation 99.9th Percentile	Post-Risk Mitigation 99.9th Percentile
U.S. Population	16%	5%
All Infants	130%	52%
Children 1-6	355%	82%
Children 7-12	258%	64%
Females 13+ , nursing	127%	40%

- The end point selected for the acute dietary assessment is cholinesterase inhibition in plasma and RBC from two acute single dose oral studies in rats (NOAEL = 0.5 mg/kg/day) based on significant inhibition at 1.0 - 1.5 mg/kg/day (LOAEL).
- The Uncertainty Factor is 100x; 10x for interspecies extrapolation and 10x for intraspecies variability. The FQPA safety factor of 10x was retained as described above.
- The acute dietary RfD is 0.005 mg/kg/day and the aPAD is 0.0005 mg/kg/day for infants, children and females from 13-50 years old.
- Exposure to chlorpyrifos can occur directly through consumption of food products and indirectly from residues in meat and milk. The acute dietary risk assessment has been extensively refined. The refined analysis conducted for chlorpyrifos includes: (1) USDA Pesticide Data Program (PDP) monitoring data which reflects the actual use of the pesticide; (2) FDA monitoring data; (3) registrant supplied market basket monitoring data (apple sauce, peanut butter, apple juice, orange juice, whole milk, ground beef and pork sausage); (4) animal feeding studies\ field trials for other commodities (almonds, walnuts, corn grain, cottonseed oil, peanut oil, sunflower oil, soybean oil, peppermint oil, spearmint oil, poultry and related products); (5) tolerance level residues (figs, dried beans, dried peas) and percent crop-treated. Monitoring data were available for nearly all commodities. See the attached Table 2 for details on what was used in the analysis for specific commodities.
- Additional monitoring data as well as additional cooking and processing studies could be used to further refine the assessment.

Chronic Dietary (Food) Risk

Chronic dietary risk is calculated by using the average consumption and residue values for foods. A risk estimate that is less than 100% of the chronic PAD (the dose at which an individual could be exposed over the course of a lifetime and no adverse health effects would be expected) does not exceed the Agency's risk concern. The cPAD is the chronic reference dose (cRfD) adjusted for the FQPA safety factor.

The chronic dietary risk (food) does not exceed the Agency's level of concern for the general U.S. population and all subgroups (i.e. <100% of the chronic PAD is utilized).

- **Based on all currently registered uses (pre-mitigation):** For the highest exposed subgroup, children 1-6 years old, 81% of the cPAD is occupied (food only). For the general U.S. population, 4% of the cPAD is occupied. See Table 3.
- **Post-mitigation:** For the highest exposed subgroup, children 1-6 years old, 51% of the cPAD is occupied (food only). For the general U.S. population, 3% of the cPAD is occupied. See Table 3.
- Chlorpyrifos is used in food handling establishments (restaurants, cafeterias, food processing facilities etc.) for the control of insects. This use was assessed in the chronic dietary assessment. The assumption was made (per current EPA policy) that ½ the limit of detection (LOD) (0.005 ppm) level residues are present in all foods that do not have a tolerance (presuming that a microencapsulated formulation is used). This is a conservative assumption. The Agency estimates that approximately 24% of all food handling establishments are treated with chlorpyrifos. Available data indicate there would be no residues greater than the LOD of 0.01 ppm on food after treatment. Based on these data the Agency believes that the risk estimates that do not include the food handling establishment use are most representative of actual, potential exposure.

TABLE 3: Chlorpyrifos: Risk Estimates as a Percentage of the Chronic PAD (% cPAD)

Sub-Population	Pre-Risk Mitigation		Post-Risk Mitigation	
	With FHE	W/O FHE	With FHE	W/O FHE
U.S. Population	4%	3%	3%	1%
All Infants	45%	33%	33%	11%
Children 1-6	81%	61%	51%	31%
Children 7-12	59%	45%	36%	21%
Females 13+ , nursing	30%	21%	20%	11%

- The toxicity endpoint selected for the chronic dietary assessment is plasma and red blood cell cholinesterase inhibition. The endpoint was selected using a weight-of-the-evidence approach from five toxicity studies. The NOAEL is 0.03 mg/kg/day.
- The Uncertainty Factor is 100x; 10x for interspecies extrapolation, and 10x for intraspecies variability. The 10x FQPA safety factor was retained as in the acute assessment.
- The chronic RfD is 0.0003 mg/kg/day. The chronic PAD is 0.00003 mg/kg/day for infants, children and females from 13-50 years old.
- The chronic dietary analysis has been extensively refined and includes: (1) USDA Pesticide Data Program (PDP) monitoring data; (2) FDA monitoring data; (3) registrant supplied market basket monitoring data; (4) animal feeding studies/field trials (almonds, walnuts, corn grain, cottonseed oil, peanut oil, sunflower oil, soybean oil, peppermint oil, spearmint oil, poultry and related products); (5) tolerance level residues (figs, dried beans, dried peas) and percent crop-treated. Monitoring data were available for nearly all commodities.
- Additional monitoring data as well as additional cooking and processing studies could be used to further refine the assessment.

Drinking Water Dietary Risk

Drinking water exposure to pesticides can occur through groundwater and surface water contamination. EPA considers both acute (one day) and chronic (lifetime) drinking water risks and uses either modeling or actual monitoring data, if available, to estimate those risks. To determine the maximum contribution from water allowed in the diet, EPA first looks at how much of the overall allowable risk is contributed by residues in food and then determines a “drinking water level of comparison” (DWLOC) to ascertain whether modeled or monitored levels exceed this level. Modeling is considered to be an unrefined assessment and provides high-end estimates.

- Drinking water concentrations for ground water were estimated using model estimates from the SCI-GROW model with the support of monitoring data; and for surface water using monitoring data. The estimated concentrations for ground water result from possible well contamination from the termiticide use as discussed below.
- Based on the conservative model estimates, a range of 0.007 ppb to 0.103 ppb was used to evaluate both acute and chronic ground water exposures.
- The monitored concentrations of chlorpyrifos in surface water range from 0.026 ppb (which represents the 95th percentile concentration) to 0.4 ppb (which represents the maximum concentration). The range of 0.026 ppb to 0.4 ppb was used for the acute assessment. The 95th percentile concentration (0.026 ppb) was used in the chronic assessment.

Acute Exposures

- The DWLOCs for acute exposure were not calculated because exposure from residential uses alone exceeded the aPAD. However, acute DWLOCs were calculated based on the risk mitigation for dietary (food) and residential exposure. The acute DWLOC for the most highly exposed subpopulation (children 1-6) is 0.9 ppb based on food and water exposures. This DWLOC is greater than the highest estimated water exposure level indicating that drinking water will fit within the acute dietary risk cup (food and water).

Chronic Exposures

- The DWLOCs for chronic exposure were not calculated because exposure from residential uses alone exceeded the cPAD. However, chronic DWLOCs were calculated based on the risk mitigation for dietary (food) and residential exposure. The chronic DWLOC for the most highly exposed subpopulation (children 1-6) is 0.15 ppb. This DWLOC is greater than the highest estimated water exposure level indicating that drinking water will fit within the chronic dietary risk cup (food and water).

TABLE 4: Drinking Water Risk Estimates

Population Subgroup	Surface Water Estimated Concentrations (ppb)	Ground Water Estimated Concentrations (excluding termiticide use) (ppb)	Acute DWLOC (ppb)	Chronic DWLOC (ppb)
U.S. Population	0.026 - 0.4 - acute 0.026 - chronic	0.007 to 0.103 (acute and chronic)	166	10
All Infants (<1 years)			2.4	0.2
Children (1 - 6 years)			0.9	0.15
Females (13 - 50 years)			9.0	0.72

Localized Well Contaminations (Termiticide Use)

- In highly localized cases there have been some instances of higher ground water concentrations observed in wells which were contaminated during termiticide treatment. Between 1992 and 1997, 251 well contaminations were reported to the Agency with the highest measured concentration being 2090 ppb. Current water standards require that contaminated well water be cleaned to 30 ppb.
- Acute exposure to chlorpyrifos in groundwater as a result of well contamination from termiticide use could potentially result in exposures of concern. However, as noted above,

the groundwater exposures from well contamination resulting from termiticide use are highly localized. Implementation of PR 96-7 for termiticides is expected to continue to significantly reduce groundwater contamination resulting from termiticide treatments. For example, incidents associated with termiticide use were 28.2 per 100,000 homes in 1997 (pre PR-96-7), and were 8.3 per 100,000 homes in 1998 (post PR-96-7).

Residential and Recreational Risk

Workers [pest control operators (PCOs) and lawn care operators (LCOs)] and homeowners can be exposed to a pesticide through mixing, loading, or applying the pesticide, and when re-entering a treated site. Risk is measured by a Margin of Exposure (MOE) which determines how close the exposure comes to the No Observed Adverse Effect Level (NOAEL) taken from animal studies. Generally, MOEs that are greater than 100 do not exceed the Agency's level of concern. However, since an FQPA safety factor of 10x has been retained for chlorpyrifos, MOEs of 1000 or greater do not exceed the Agency's level of concern for homeowners. For professional (worker) applicators, MOEs of 100 or greater do not exceed the Agency's level of concern since the 10x FQPA safety factor does not apply to workers.

- For the short-term dermal toxicity endpoint, a NOAEL of 5.0 mg/kg/day based on plasma and RBC cholinesterase inhibition observed at the LOAEL of 10 mg/kg/day, was used. It was taken from a 21-day dermal toxicity study in rats; therefore, no dermal absorption factor was needed.
- For the intermediate- and long-term dermal toxicity endpoint, a NOAEL of 0.03 mg/kg/day was selected from five oral toxicity studies using a weight-of-the-evidence approach. Dermal absorption was estimated to be 3 percent based on the ratio of the oral LOAEL of 0.3 mg/kg/day from the rat developmental neurotoxicity study to the dermal LOAEL of 10 mg/kg/day from the 21-day dermal study.
- For the short- and intermediate-term inhalation toxicity endpoint, a NOAEL of 0.1 mg/kg/day was selected using two separate 90-day rat inhalation studies that did not show effects at the highest dose tested. This dose reflected the highest achievable chlorpyrifos air concentration (i.e. air saturated with chlorpyrifos).
- For the long-term inhalation toxicity endpoint, a NOAEL of 0.03 mg/kg/day was selected from five oral toxicity studies using a weight-of-the-evidence approach. It was assumed that inhalation and oral absorption are equivalent.
- The acute oral end point is cholinesterase inhibition in plasma from an acute blood time course study in male rats (NOAEL = 0.5 mg/kg/day) based on 28-40% inhibition at peak time of inhibition (3-6 hours post-exposure) at 1 mg/kg/day. The acute oral NOAEL was used to assess short-term exposures resulting from incidental ingestion (i.e., hand to mouth exposures) of less than one week for children.

- The exposure duration for short-term assessments is 1 to 30 days. Intermediate-term durations are 1 month to six months, and long-term exposures are durations greater than six months.
- Four of the residential post-application scenarios and one residential applicator scenario were assessed using chlorpyrifos-specific studies submitted by the registrant. In the absence of chlorpyrifos-specific studies, the other exposures were estimated using the draft SOPs for residential exposure assessments. In some cases, chlorpyrifos-specific studies were supplemented by the SOPs.
- There are a number of residential uses for chlorpyrifos including use as a termiticide, a lawn treatment, an ornamental treatment, indoor crack & crevice and spot treatment, and in pet collars. In many cases, these can be applied by homeowners. Chlorpyrifos is also used on golf courses and as a mosquitocide, which can result in residential or recreational exposures.

A. Residential and Handler Post-Application Risks (Except Termiticide Use)

- **Based on all currently registered uses (pre-mitigation):** Residential post-application exposures are of concern for uses including lawn treatments, crack & crevice treatments, perimeter treatments, and pet collars. All scenarios where residents mix/load/apply chlorpyrifos products are of concern with the exception of a limited spot application scenario.
- The risks for residential and recreational uses are mitigated by:
 - Eliminating all indoor residential uses (except fully contained ant baits in child resistance packaging).
 - Eliminating all outdoor residential uses (except limited public health uses).
 - Eliminating all indoor and outdoor non-residential uses except:
 - Use on golf courses
 - Limited public health uses (i.e. mosquito control and fire ant mounds)
 - Limited use in industrial settings (e.g. manufacturing plants, ship holds)
 - 2-1-01---- Last date for distribution\sale by registrants.
 - 12-31-01---- Last date for sale of products by retailers.
 - Reducing the maximum application rate for golf course to from 4 lb a.i./A to 1 lb. a.i./A.
- **Post-mitigation:** The proposed risk mitigation would address all residential and recreational risks of concern. See Table 5.

**TABLE 5: Non-Termiticide Residential and Recreational Risk Estimates
(Target MOE=1000)**

Exposure Scenario	Pre-Mitigation MOEs		Post-Mitigation MOEs	
	Adult	Child	Adult	Child
Post-Application				
Indoor Crack and Crevice (Short-Term)1	390	110	Use removed	
Lawn Treatment (Liquid) (Short-Term)2	9 - 96 (Max rate - Min. rate)	7.5 - 60 (Max rate - Min. rate)	Use removed	
Lawn Treatment (Granular) (Short-Term)3	110	73	Use removed	
Pet Collar Use (Long-Term)4	670 (dog) 2500 (cat)	140 (dog) 530 (cat)	Use removed	
Golf Course	600	360 (adolescent golfer)	2400	1500
Mosquito Control	43,000	15,000	Not Applicable	
Residential Mixer/Loader/Applicator				
Indoor Crack and Crevice	100 (0.5% product) 200 (1% Product) 1600 (2 oz. Spot treatment)	Not Applicable	Use removed	
Broadcast Turf (Liquid) (Hose-end Sprayer)	6 - 23 (Max. And Min. Dilution Rates)		Use removed	
Turf Spot Treatment (Liquid) (Low Pressure Handwand)	37-150 (Max. And Min. Dilution Rates)		Use removed	
Broadcast Turf (granular) (hand application)	17		Use removed	
Broadcast Turf (granular) (Belly Grinder)	3 24 (spot treatment)		Use removed	
Broadcast Turf (granular) (Push-type Spreader)	110		Use removed	
Ready-to-Use Perimeter Treatment	625		Use removed	

Exposure Scenario	Pre-Mitigation MOEs		Post-Mitigation MOEs	
	Adult	Child	Adult	Child
Ornamental Application (Hose-end Sprayer)	28 - 880 (max. and min. dilution rates)		Use removed	
Ornamental Application (Low Pressure Handwand)	8 - 270 (max. and min. dilution rates)		Use removed	
Dust Application	250		Use removed	
Paint Brush Application	35 (1 gal.) 140 (1 qt.)		Use removed	

B. Residential Post-Application Risks (Termiticide Use)

- The risk mitigation for residential risk concerns posed by the termiticide use patterns will be mitigated by:
 - Eliminating whole house “post-construction” termiticide use.
 - Phasing out limited post-construction spot and local termiticide treatments by 2002.
 - Phasing out pre-construction termiticide treatments by 2005.
- The Agency conducted an assessment of termiticide post-application risks based on a chlorpyrifos-specific study submitted by DAS. This study collected air measurements from the kitchen, bedroom and basement of 31 homes for up to 1 year following a termiticide treatment. Four types of housing structures were evaluated which include: basement, slab, crawlspace, and plenum-type structures. This study evaluated treatment of existing homes, referred to as post-construction treatment. Applications were conducted according to the label-recommended rate of approximately 1% active ingredient.
- Inhalation exposure is the primary concern with the termiticide treatment. Chlorpyrifos gets into the home through cracks in the foundation or slab, and by diffusing through building materials. Incremental time-weighted average (TWA) air concentrations were calculated for the entire house, assuming an individual could be in any room. Based on the mitigation plan, the TWA concentrations were normalized to a reduced application rate of 0.5% ai. As part of risk characterization, the Agency evaluated both intermediate and long-term exposures due to uncertainties related to the toxicity endpoints for both durations.

- For children, all of the 90-day median MOEs are greater than 1000 (MOEs range from 1,900 to 3,800), and therefore do not exceed a level of concern. However, some of the 1-year median MOEs are below 1000, and therefore exceed the level of concern (MOEs range from 530 to 1,100). The lowest 90-day and 1-year MOEs for an individual house are 440 and 270, respectively. It should be noted that the 90 day risk estimates may be underestimated, while the 1 year risk estimates may be overestimated based on the uncertainties discussed later in this section. However, it is expected that the risks are bounded by the ranges presented. See Table 6 below.

TABLE 6: Termiticide Post-Application Risk Estimates (mitigated application rate of 0.5%) Target MOE=1000

Home Construction Type	Range of MOEs (90-Day TWA*)	Range of MOEs (1-Year TWA)
Basement	600 - 8700 (median = 3800)	270 - 2500 (median = 1100)
Crawlspace	950 - 7200 (median = 2100)	340 - 2100 (median = 530)
Slab	440 - 5800 (median = 1900)	280 - 2200 (median = 600)
Plenum	460 - 6400 (median = 1900)	270 - 2700 (median = 760)

*Time weighted average

- There are a number of uncertainties in the termiticide risk estimates that arise from the following sources: choice of toxicological data used to establish the inhalation endpoint, chlorpyrifos air concentrations, and exposure assumptions.

Toxicity: There are uncertainties associated with both the intermediate and long-term endpoints. The ideal data are not available. The intermediate endpoint is based on two inhalation studies, which matches the exposure route of concern. However, the exposure time is too short compared to termiticide exposures because rats were only exposed for 6 hours/day, 5 days per week. The long-term endpoint is based on oral studies which introduces uncertainties, primarily because of route-to-route extrapolation. In addition, there is a large difference between the effect level and the no observable effect level. This difference effectively provides an additional 3 to 10 fold cushion to the risk estimates.

Air Concentrations: The available data suggest that temperature influences indoor chlorpyrifos concentrations resulting from termiticide treatments. For example, warmer temperatures are associated with higher concentrations. In the DAS study, 26 of 31 homes were from the South or warm climates. Therefore, the air

concentrations from these homes may represent high-end estimates, that could overestimate exposures for treated houses in more temperate climates.

Exposure Assumptions. The assumptions used to estimate exposures are based on USEPA recommended values (Exposure Factors Handbook), and are designed to be conservative for the majority of the population. For example, this assessment assumed that children aged 1-6 years are exposed to chlorpyrifos air concentrations in a treated home for 20 hours/day, 7 days/week, for up to one year.

- In summary, it is important to bear in mind that FQPA demands that stringent safety standards be used to assess residential uses, including termiticide uses. Although not all of the risk estimates achieve a margin of exposure of 1000, the Agency believes that considering the uncertainties in the assessment (the conservative assumptions, the 1000 fold safety factor, in conjunction with the additional 3 to 10 fold cushion between the effect level and the no observable effect level), as well as the mitigation, this use does not raise a concern.
- The mitigation measures discussed at the beginning of this section will further reduce exposures and risk. For example, the removal of whole house barrier treatment addresses the exposures of most concern. It is expected that the limited spot and local, and the pre-construction treatments would represent less exposure.

C. Professional (Worker) Mixer/Loader/Applicator Residential Risk Estimates

- Risks to PCOs who mix, load and apply were estimated for 10 main scenarios, some of which included a range of possible exposures and durations (e.g. termiticides), each having a separate Margin of Exposure (MOE) calculation. For the PCOs, an MOE greater than 100 is not of concern to the Agency. Table 7 summarizes the scenarios with total MOEs for each scenario evaluated where ST = short-term, IT = intermediate-term and LT = long-term.
- Ranges of MOEs are provided for a number of scenarios. These ranges usually reflect a range of possible application rates ranging from the label maximum to what might be considered “typical” or minimum use rates. They may also reflect different data sources or active ingredient concentrations.
- It should be noted that many of the scenarios presented below will be mitigated or removed as a result of the risk mitigation proposal. These mitigated or removed scenarios are marked by an * in Table 7 below.

Table 7: Professional Handler Risk Summary

Application Scenario	Clothing	Data Source	MOE
(1) Indoor Crack & Crevice Treatment*			
Long term PCO Applicator (0.29% chlorpyrifos)	double layer clothes, chemically-resistant boots and gloves, eye protection	Biomonitoring study (minimum, mean and maximum amount handled)	13 (max) 45 (mean) 4500 (min)
(2) Broadcast Turf Application (Intermediate and Long-Term)*			
Applicator (1 or 4 lb ai/Acre)	single layer clothes, chemically-resistant knee high boots and gloves, hat (knee high boots not required by label)	Biomonitoring Study (25% of label maximum rate or adjustment for label-recommended max application rate)	75 (Biomonitoring)
			20 (Label max)
Mixer/Loader (liquid)	single layer clothes, gloves	PHED V1.1 (biomonitoring study rate and 25% of maximum label rate)	170-680 100-380
	double layer clothes, gloves		200-820 100 -420
(3) Golf Course Use (Short-term) (Range from Maximum to Minimum Application Rates)*			
Mixer/Loader (Liquid)	LS, LP, gloves	PHED V1.1	26-100
Mixer/Loader (Wettable Powder in water soluble bags)	LS, LP, gloves	PHED V1.1	100-400
Groundboom Applicator	LS, LP, no gloves	PHED V1.1	43-170
		Biomonitoring	15-63
Mix/Load/Apply via Handgun (greens/tees) (Liquid)	LS, LP, gloves	PHED V1.1	36-140
(4) Insecticidal Dust Product (Shaker Can or Bulbous Duster)*			
Worker (7% ai chlorpyrifos; 7.91 or 198 g ai)			

Application Scenario	Clothing	Data Source	MOE
Short- term	LS, LP, gloves	Scientific Literature Study	98 (7.9 g) 3.9 (198 g)
Intermediate term			20 (7.9 g) 0.8 (198 g)
(5) Granular Formulation (Hand Application) (2 lb ai/acre)*			
LCO (intermediate-term)	LS, LP, gloves	PHED V1.1	20
	Double layer clothing, gloves		34
(6) Granular Formulation (Belly Grinder) (2 lb ai/acre)*			
LCO (intermediate-term)	LS, LP, gloves	PHED V1.1	7
	Double layer clothing, gloves		11
(7) Granular Formulation (Push-type Spreader) (2 lb ai/acre)*			
LCO (intermediate-term)	LS, LP, gloves	PHED V1.1	54
	Double layer clothing		92
Termiticide Treatments			
(8) Pre-Construction (1.44% chlorpyrifos) (long-term)*			
Mixer/Loader/ Applicator (3 hour average exposure)	label-specified PPE: single layer clothes and forearm-length chemically-resistant gloves (forearm length gloves not required by label)	Dosimetry and air monitoring from study	15
	double layer clothes (LS, LP, coveralls, rubber boots, and forearm-length gloves) (forearm-length gloves not required by label)		33

Application Scenario	Clothing	Data Source	MOE
Tarp puller	with forearm-length gloves (LS, LP, leather and/or rubber boots and hat)	Dosimetry and air monitoring from study (1-8 tarps)	87 (8 tarps) 690 (1 tarp)
	without gloves (LS, LP, leather and/or rubber boots and hat)		39 (8 tarps) 310 (1 tarp)
(9) Post-Construction (1% chlorpyrifos) (long-term)*			
Mixer/Loader/ Applicator	Label-specified PPE: LS, LP, chemically resistant gloves, hat, eye protection and half face piece respirator in confined spaces; During M/L: 2 layers clothes and chemically-resistant shoes	Biomonitoring: 4.3 (n=5)	7
		Dosimetry and air monitoring (n=14)	9
(10) Mosquitocide Mixer/Loader/Applicator (PHED V1.1) (Short- and intermediate-term)			
Mixer/Loader-- Aerial	PPE double layer clothes and gloves	PHED V1.1	26 14
	Engineering Controls (enclosed cockpit) single layer clothes and gloves		160 43
Mixer/Loader-- Ground-based fogger	PPE, single layer clothes and gloves		280 133
	engineering controls (enclosed cab) and single layer clothes and gloves		250
Aerial Applicator	engineering controls (enclosed cockpit) and single layer clothes and no gloves		240 71

Application Scenario	Clothing	Data Source	MOE
Ground-based fogged Applicator	engineering controls (enclosed cab) and single layer clothes and no gloves		280-560
			100-200

LS=Long sleeves; LP = Long pants; SS = short sleeves; SP = short pants
H2O = water; ST = short-term (1- 30 days); IT = intermediate term (30 days to 6 months) LT = long term (> 6 months)

Aggregate Risk

Aggregate risk is defined as the combined risk from exposure through food, drinking water, and residential uses.

Short-Term, and Intermediate-Term

- The short-term and intermediate-term aggregate risks were not originally calculated for chlorpyrifos because the risks from residential exposure alone exceeded the Agency's level of concern based on currently registered uses. However, aggregate risk estimates were calculated based on the proposed risk mitigation for dietary (food) and residential exposure.
- Based on the mitigation, the Agency has aggregated remaining exposures from food, drinking water, mosquitocide applications and golf course uses. The short-term and intermediate-term aggregate risks do not exceed the Agency's level of concern when the proposed mitigation is accounted for in the assessment.

Long-Term

- Long-term aggregate risk was not originally calculated for chlorpyrifos because the risks from residential exposure alone exceeded the Agency's level of concern based on currently registered uses. However, aggregate risk estimates were calculated based on risk mitigation for dietary (food) and residential exposure.
- Based on the mitigation, the Agency has aggregated remaining exposures from food and drinking water. The long-term aggregate risks do not raise a concern when the uncertainties in the assessment and the proposed mitigation are considered.

Occupational (Agricultural) Risk

Workers can be exposed to a pesticide through mixing, loading, or applying the pesticide, and re-entering a treated site. Worker risk is measured by a Margin of Exposure (MOE) which determines how close the occupational exposure comes to the No Observed Adverse Effect Level (NOAEL) taken from animal studies. Generally, MOEs that are greater than 100 do not exceed the Agency's level of concern. For workers entering a treated site, Restricted Entry Intervals (REIs) are calculated to determine the minimum length of time required before workers or others are allowed to enter.

Occupational risk estimates associated with mixing, loading and application are of concern for most exposure scenarios. The post-application risks to reentry workers also are of concern based on current REIs and application rates for cauliflower, tree nuts, tree fruits, and citrus. To achieve MOEs that are not a concern for post-application workers, some REIs would need to be increased in length. The necessary changes to REIs have been agreed to as part of the mitigation plan.

- For the short-term dermal toxicity endpoint, a NOAEL of 5.0 mg/kg/day based on plasma and RBC cholinesterase inhibition at the LOAEL of 10 mg/kg/day, was used. It was taken from a 21-day dermal toxicity study in rats; therefore, no dermal absorption factor was needed.
- For the short-term inhalation toxicity endpoint, a NOAEL of 0.1 mg/kg/day was selected from two separate 90-day rat inhalation studies in which effects were not observed at the highest dose tested.
- The exposure duration for short-term assessment is 1 to 30 days, which covers the expected exposure duration for mixer/loader/applicators.

Mixer/Loader/Applicator Risk Estimates

- Sixteen exposure scenarios were identified. These are listed in Table 7 below.
- Chlorpyrifos-specific exposure data were available for the exposure assessments for several mixer/loader/applicator scenarios (1a, 1b, 1c, 2b, 3b, 5, 6, 7, 12, 13, 14) . Exposure assessments were made using the Pesticide Handlers Exposure Database (PHED) Version 1.1 for the other scenarios and where additional risk mitigation was necessary for the scenarios that used chemical-specific data..
- The PPE assumed for each scenario is:
 - Footwear, coveralls, long-sleeve shirt, long pants, dust-mist respirator (scenarios 7, 10, 11)
 - Footwear, chemical resistant gloves, coveralls, long-sleeve shirt, long pants, dust-mist respirator (all other scenarios)
- The engineering controls and associated PPE assumed for each scenario are listed below:

- Footwear, chemical resistant gloves, long-sleeve shirt, long pants, closed mixing\loading system. (scenarios 1a,1b,1c, 2a, 2b, 2c, 3a, 3b)
- Footwear, long-sleeve shirt, long pants, enclosed cab\cockpit (scenarios 4a, 4b, 5, 6, 7, 10,11)

- The combined dermal and inhalation risks were calculated based on the maximum PPE and/or engineering controls described above. In all cases, most of the risk results from dermal exposure.

TABLE 8: Agricultural Worker M/L/A MOEs

Exposure Scenario (Scenario #)	Application Rates (lb ai/acre)	Short-Term Total MOEs	
		PPE	Engineering Controls
Mixer/Loader Exposure			
Mixing/Loading Liquids for Aerial/Chemigation Application (1a)	1.5 cranberries, corn	23	52
	3.5 citrus	34	78
Mixing/Loading Liquids for Groundboom Application (1b)	1.5 predominant max	100	Target Reached w/ PPE
	5.0 tobacco max	30	69
	2.0 Sodfarm (includes tobacco and potatoes)	75	170
	4.0 Sodfarm	38	86
	8.0 sodfarm fire ants	150	Target Reached w/ PPE
Mixing/Loading Liquids for Airblast Application (1c)	2.0 predominant max such as Fruits & Nuts	150	Target Reached w/ PPE
	6.0 citrus	100	Target Reached w/ PPE
Mixing WP for Aerial/Chemigation Application (2a)	2.0 predominant max (orchards)	Open Bags Not Supported	23
	3.5 citrus		46
Mixing WP for Groundboom Application (2b)	1.0 predominant max (brassica)		200
	4.0 soil treatment ornamentals outdoors		400
	1.3 & 3.0 Sodfarm		150 / 67
	8.0 sodfarm fire ants (harvest only)		200
Mixing WP for Airblast Application (2c)	2.0 predominant max		200

Exposure Scenario (Scenario #)	Application Rates (lb ai/acre)	Short-Term Total MOEs	
		PPE	Engineering Controls
	6.0 citrus		130
Loading Granulars for Aerial Application (3a)	1.95 maximum aerial rate	25	270
Loading Granulars for Ground Application (3b)	1.0 typical corn	210	Target Reached w/ PPE
	2.0 max corn	110	Target Reached w/ PPE
	3.0 maximum ground rate (tobacco)	71	110
Applicator Exposure			
Aerial (Spray) -- Enclosed Cockpit (4a)	2.0 predominant max	NE	60
	3.5 citrus	NE	120
Aerial (Granulars) -- Enclosed Cockpit (4b)	1.95	NE	8
Groundboom Tractor (5)	1.5 predominant max	Biomonitoring data indicate that open cabs are insufficient	410
	5.0 tobacco max		120
	4.0 Sodfarms		150
	8.0 Sodfarms fire ants		610
Airblast Applicator (6)	2.0 predominant max	Biomonitoring data indicate that open cabs are insufficient	110
	6.0 citrus		70
Tractor-Drawn Granular Spreader (7)	1.0 typical corn	270	Target Reached w/ PPE
	2.0 max corn	140	Target Reached w/ PPE
	3.0 maximum ground rate (tobacco)	90	110
Seed Treatment (8)	No Data	No Data	No Data
Dip Application (Preplant Peaches) (9)	No Data	No Data	No Data
Flagger Exposure			
Spray Applications (10)	2.0 predominant max	37	880
	3.5 citrus	74	1800
Granular Applications (11)	1.95	170	Target Reached w/ PPE
Mixer/Loader/Applicator Exposure			

Exposure Scenario (Scenario #)	Application Rates (lb ai/acre)	Short-Term Total MOEs	
		PPE	Engineering Controls
Backpack Sprayer (12)	0.0417 lb ai/gal predominant max / 0.08 lb ai/gal bark beetle treatment / 0.03 lb ai/gal stump treatment	110 / 58 / 150	Target Reached w/ PPE except for higher concentration bark beetle treatment
	3.5 citrus bark	53	Not Feasible
	0.039 lb ai/gal / 750 ft ²	3500	Target Reached w/ PPE
Low Pressure Handwand (13)	0.0417 predominant max / 0.08 lb ai/gal bark beetle treatment / 0.03 lb ai/gal stump treatment	310 / 160 / 440	Target Reached w/ PPE
	3.5 citrus bark	150	Target Reached w/ PPE
	0.039 lb ai/gal / 750 ft ²	10,000	Target Reached w/ PPE
High Pressure Handwand (greenhouse uses) (14)	Min. 0.0033 lb ai/gal	38	Not Feasible
	Max. 0.0066 lb ai/gal	19	Not Feasible
Hydraulic Hand-held Sprayer for Bark / Pine Seedling Treatment (15)	3.5 citrus bark	14	Not Feasible
	0.08 lb ai/gal bark beetle treatment / 0.16 lb ai/ gal pine seedling treatment	12 / 6	Not Feasible
	0.039 lb ai/gal / 750 ft ² (animal premise)	1,900	Target Reached w/ PPE
Dry Bulk Fertilizer Impregnation (16)	1.0 lb ai / 200 lb fertilizer /acre	No Data	No Data

NE = Not evaluated

predominant maximum = maximum application on most labels for most crops

- In some cases the same person may mix, load and apply the chemical (e.g. groundboom and airblast). In these cases, the estimated combined risk will be higher.

Post-Application Risk Estimates

There is potential exposure to persons entering treated sites (e.g., scouts and harvesters) after application is complete. Post-application exposure data have been required. Although several studies have been submitted, the use of standard transfer coefficients (Tc) was still necessary to represent some crops. Dislodgeable foliar residue (DFR) values are based on chlorpyrifos-specific studies.

- Chlorpyrifos use patterns show that both short-term (1 to 30 days) and intermediate-term (1 month to 6 months) exposure is possible for post-application exposures. Therefore, risk

estimates were calculated for both short-term and intermediate-term exposures. The most sensitive assessment (intermediate-term) is reflected in the calculated restricted entry intervals (REIs).

- In some of the chlorpyrifos-specific studies, the dermal exposure levels were monitored concurrently with the DFR levels (scouting cauliflower and tomatoes and citrus harvesting/pruning). These transfer coefficients were used to estimate the REIs for these crops. The citrus transfer coefficients were used as a surrogate for harvesting/pruning activities for all tree nuts and tree fruit. The cauliflower scouting data were used as a surrogate for all other scouting activities. Agency standard transfer coefficients were used for all other post application activities.
- DFR data were submitted for sugar beets, sweet corn, cotton, citrus, almonds, apples, pecans, tomatoes and cauliflower. Eight of the nine crops indicated a rapid decline over the first 24 hours. Cauliflower DFR data did not indicate this rapid decline resulting in the longer REIs for that crop.
- For worker re-entry risk, the calculated REI represents the day on which the MOE is greater than or equal to 100.
- The following tables summarize the restricted entry intervals calculated for chlorpyrifos.

Table 9: Post-application Worker Risk Estimates: Restricted-Entry Intervals

Crops	Scouting	Harvesting
All Crops (except as noted)	24 hours	24 hours (48 hours sweet potatoes)
Cauliflower	3 days	10 days
Citrus	2 days	5 days
Nut Trees	2 days	2 days
Fruit Trees	1 day	4 days

- The registrant/Agency is proposing to mitigate occupational post-application risk concerns by amending labels to reflect the REIs for harvesters as outlined above.

Ecological Risk Assessment

To estimate potential ecological risk, EPA integrates the results of exposure and ecotoxicity using the quotient method. Risk quotients (RQs) are calculated by dividing exposure estimates by

ecotoxicity values, both acute and chronic, for various species. Risk characterization provides further information on the likelihood of adverse effects occurring by considering the fate of the chemical in the environment, communities and species potentially at risk, their spatial and temporal distributions, and the nature of the effects observed in studies. The higher the RQ the greater the concern.

Nontarget Terrestrial Animal Risk

- Avian RQs indicate risks of concern for both acute (0.05 to 11) and chronic exposure (0.28 to 58) for most uses and use rates. Three field studies as well as some wildlife incidents support these findings.
- Mammalian RQs indicate risks of concern for both acute (0.002 to 14) and chronic exposure (0.7 to 140) for most uses and use rates for small and medium-sized animals. Three field studies support these findings.
- Chlorpyrifos is highly toxic to honey bees and field studies indicate that bees and pollinators are at risk if present during spray applications.

Nontarget Aquatic Animal Risk

- Freshwater and estuarine/marine fish RQs indicate risks of concern for both acute (0.77 to 35) and chronic exposure (1.1 to 100) for all outdoor uses. Fish kills reported in 2 of 3 field studies provide support for acute risks to fish.
- Freshwater and estuarine/marine invertebrate RQs indicate risks of concern for both acute (14 to 9,700) and chronic exposure (15 to 76,100) for all outdoor uses.

Summary

Chlorpyrifos use poses acute and reproductive risks to many nontarget aquatic and terrestrial animals for all outdoor uses assessed. In general, risk estimates are of greater concern for aquatic species. Among aquatic species, there is greater concern for estuarine than freshwater species.

Summary of Pending Data

- The Agency is currently reviewing a recently received toxicology study on chlorpyrifos-oxon (a degradate), and a biomonitoring study which measures TCP (a degradate) levels in children. The Agency has also received a new toxicity study using human volunteer test subjects. This submission is not complete and has not been reviewed. A drinking water

monitoring study has been conducted by a group of five registrants for five organophosphate pesticides including chlorpyrifos. The Agency is currently reviewing these data.

Summary of Public Comments

- Over 4,000 comments were received by the Agency during the Phase 3 public comment period.
- Registrant comments were primarily concerned with the selection of toxicological endpoints, determination of the FQPA safety factor, not using human toxicology studies in the assessment and not using probabilistic methods for the ecological risk assessment.
- Comments from growers, commodity groups, pest control advisors/crop consultants, pesticide retailers and PCOs/PCO groups stressed the importance of chlorpyrifos in Integrated Pest Management (IPM) programs, the effectiveness of the pesticide, the economic advantages of its use, and the lack of equivalent alternatives in some cases. These comments have been provided to the Biological and Economic Analysis Division.
- Comments from environmental and consumer organizations and persons who believe they have become ill as a result of chlorpyrifos use focused on the risks associated with residential uses of chlorpyrifos, determination of the FQPA safety factor, toxicological effects, aggregate and cumulative assessments and trichloropyridinol (TCP), the primary degradate of chlorpyrifos.